**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**In re the application of:** Luithle *et al.*

**Serial No.:** 10/516,777

**Filed:** January 13, 2006

**For:** 2-HETEROARYL CARBOXAMIDES

**Attorney Docket No.:** LeA36131 [84804(303989)]

**Confirmation No.:** 5263

**Group Art Unit:** 1625

**Examiner:** John Mabry

Mail Stop: Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

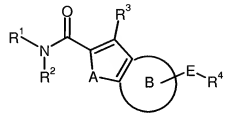
## RESPONSE TO FINAL OFFICE ACTION

Dear Commissioner:

In response to the Office Action mailed July 27, 2010 Applicant hereby submits the following remarks. A Notice of Appeal and a Petition for Extension of Time for three (3) months, from October 27, 2010, to and including January 27, 2011 is submitted herewith.

## Listing of the Claims

1. (Previously Presented) A compound of formula (I):




(I),

in which

$R^1$ is 1-azabicyclo[2.2.2]oct-3-yl, which is optionally substituted via the nitrogen atom by a radical selected from the group of $C_1$-$C_4$-alkyl, benzyl and oxy,

$R^2$ is hydrogen or $C_1$-$C_6$-alkyl,

$R^3$ is hydrogen, halogen or $C_1$-$C_6$-alkyl,

$R^4$ is hydrogen, halogen, cyano, amino, trifluoromethyl, trifluoromethoxy, $C_1$-$C_6$-alkyl, $C_1$-$C_6$-alkylcarbonyl, $C_1$-$C_6$-alkylamino, formyl, hydroxycarbonyl, $C_1$-$C_6$-alkoxy, $C_1$-$C_6$-alkoxycarbonyl, $C_1$-$C_6$-alkylthio, $C_1$-$C_6$-alkylcarbonylamino, $C_1$-$C_6$-alkylaminocarbonyl, $C_1$-$C_4$-alkylsulphonylamino, $C_3$-$C_8$-cycloalkylcarbonyl-amino, $C_3$-$C_6$-cycloalkylaminocarbonyl, pyrrolyl, $C_1$-$C_6$-alkylaminocarbonylamino, hydroxyl, phenyl morpholinyl, oxypiperidinyl, oxopyrrolidinyl, oxomorpholinyl, pyrrolidinyl, morpholinylcarbonyl, piperidinyl, pyridinyl, dihydropyrrolylcarbonyl, $C_1$-$C_6$-alkylpiperizinylcarbonyl,

isoxazolecarbonylamino, tetrahydrofuranylcarbonylamino, furoylamino, piperidinylcarbonyl, or piperidinylcarbonyl ,

where $C_1$-$C_6$-alkyl may optionally be substituted by hydroxyl, cyano, amino, $C_1$-$C_6$-alkylaminocarbonylamino, $C_1$-$C_6$-alkylaminocarboxyl, morpholinyl or aryl,

$C_1$-$C_6$-alkylaminocarbonyl may optionally be substituted by $C_1$-$C_6$-alkoxy or $C_1$-$C_6$-alkylamino, and

$C_1$-$C_6$-alkylcarbonylamino may optionally be substituted by $C_1$-$C_6$-alkoxy,

A is oxygen or sulphur,

the ring B is benzo or pyrido, each of which are optionally substituted by radicals from the series halogen, cyano, formyl, trifluoromethyl, trifluoromethoxy, nitro, amino, $C_1$-$C_6$-alkyl and $C_1$-$C_6$-alkoxy,

and

E is C≡C, phenylene, thienylene, oxadizolylene, pyrrolylene, furanylene, pyrimidinylene, or pyridinylene wherein each ring system respectively may be substituted by radicals from the series halogen, cyano, trifluoromethyl, trifluoromethoxy, nitro, amino, $C_1$-$C_6$-alkoxy and $C_1$-$C_6$-alkyl,

or a salt thereof.

2. (Previously Presented) The compound of formula (I) of Claim 1, in which

$R^1$ is 1-azabicyclo[2.2.2]oct-3-yl,

$R^2$ is hydrogen or $C_1$-$C_4$-alkyl,

$R^3$ is hydrogen, fluorine, chlorine, bromine or $C_1$-$C_4$-alkyl,

$R^4$ is hydrogen, fluorine, chlorine, bromine, cyano, amino, trifluoromethyl, trifluoromethoxy, $C_1$-$C_4$-alkyl, $C_1$-$C_4$-alkylcarbonyl, $C_1$-$C_4$-alkylamino, formyl, hydroxycarbonyl, $C_1$-$C_4$-alkoxy, $C_1$-$C_4$-alkoxycarbonyl, $C_1$-$C_4$-alkylthio, $C_1$-$C_4$-alkylcarbonylamino, $C_1$-$C_4$-alkylaminocarbonyl, $C_1$-$C_4$-alkylsulphonylamino, $C_3$-$C_6$-cycloalkylcarbonylamino, $C_3$-$C_6$-cycloalkylaminocarbonyl, pyrrolyl, $C_1$-$C_4$-alkylaminocarbonylamino, hydroxyl, phenyl morpholinyl, oxypiperidinyl, oxopyrrolidinyl, oxomorpholinyl, pyrrolidinyl, morpholinylcarbonyl, piperidinyl, pyridinyl, dihydropyrrolylcarbonyl, $C_1$-$C_4$-alkylpiperizinylcarbonyl, isoxazolecarbonylamino, tetrahydrofuranylcarbonylamino, furoylamino, piperidinylcarbonyl, or piperidinylcarbonyl ,

where $C_1$-$C_4$-alkyl may optionally be substituted by hydroxyl, cyano, amino, $C_1$-$C_4$-alkylaminocarbonylamino, $C_1$-$C_4$-alkylaminocarboxyl, morpholinyl or aryl,

$C_1$-$C_4$-alkylaminocarbonyl may optionally be substituted by $C_1$-$C_4$-alkoxy or $C_1$-$C_4$-alkylamino, and

$C_1$-$C_4$-alkylcarbonylamino may optionally be substituted by $C_1$-$C_4$-alkoxy,

A is oxygen or sulphur,

the ring B is benzo or pyrido, each of which are optionally substituted by radicals from the series halogen, cyano, trifluoromethyl, trifluoromethoxy and $C_1$-$C_4$-alkyl,

and

E is C≡C, phenylene, thienylene, oxadizolylene, pyrrolylene, furanylene, pyrimidinylene, or pyridinylene wherein each ring system respectively may be substituted by radicals from the series halogen, cyano, trifluoromethyl, trifluoromethoxy, nitro, amino, $C_1$-$C_4$-alkoxy and $C_1$-$C_4$-alkyl,

or a salt thereof.

3. (Previously Presented) The compound of formula (I) of Claim 1, in which

$R^1$ is 1-azabicyclo[2.2.2]oct-3-yl,

$R^2$ and $R^3$ are hydrogen,

$R^4$ is hydrogen, fluorine, chlorine, bromine, cyano, amino, trifluoromethyl, trifluoromethoxy, $C_1$-$C_4$-alkyl, $C_1$-$C_4$-alkylcarbonyl, $C_1$-$C_4$-alkylamino, formyl, hydroxycarbonyl, $C_1$-$C_4$-alkoxy, $C_1$-$C_4$-alkoxycarbonyl, $C_1$-$C_6$-alkylthio, $C_1$-$C_4$-alkylcarbonylamino, $C_1$-$C_4$-alkylaminocarbonyl, $C_1$-$C_4$-alkylsulphonylamino, $C_3$-$C_6$-cycloalkylcarbonylamino, $C_3$-$C_6$-cycloalkylaminocarbonyl, pyrrolyl, $C_1$-$C_4$-alkylaminocarbonylamino, hydroxyl, phenyl morpholinyl, oxypiperidinyl, oxopyrrolidinyl, oxomorpholinyl, pyrrolidinyl, morpholinylcarbonyl, piperidinyl, pyridinyl, dihydropyrrolylcarbonyl, $C_1$-$C_4$-alkylpiperizinylcarbonyl, isoxazolecarbonylamino, tetrahydrofuranylcarbonylamino, furoylamino, piperidinylcarbonyl, or piperidinylcarbonyl ,

where $C_1$-$C_4$-alkyl may optionally be substituted by hydroxyl, cyano, amino, $C_1$-$C_4$-alkylaminocarbonylamino, $C_1$-$C_4$-alkylaminocarboxyl, morpholinyl or aryl,

$C_1$-$C_4$-alkylaminocarbonyl may optionally be substituted by $C_1$-$C_4$-alkoxy or $C_1$-$C_4$-alkylamino, and

$C_1$-$C_4$-alkylcarbonylamino may optionally be substituted by $C_1$-$C_4$-alkoxy,

A is oxygen,

the ring B is benzo or pyrido, each of which are optionally substituted by radicals from the series halogen, cyano, trifluoromethyl, trifluoromethoxy and $C_1$-$C_4$-alkyl,

and

E is C≡C, phenylene, thienylene, oxadizolylene, pyrrolylene, furanylene, pyrimidinylene, or pyridinylene wherein each ring system respectively may be substituted by radicals from the series halogen, cyano, trifluoromethyl, trifluoromethoxy, nitro, amino, $C_1$-$C_4$-alkoxy and $C_1$-$C_4$-alkyl,

or a salt thereof.

4. (Currently Amended) A compound of formula (I) of Claim 1, in which

$R^1$ is 1-azabicyclo[2.2.2]oct-3-yl,

$R^2$ is hydrogen or $C_1$-$C_6$-alkyl,

$R^3$ is hydrogen, halogen or $C_1$-$C_6$-alkyl,

$R^4$ is hydrogen, halogen, cyano, amino, trifluoromethyl, trifluoromethoxy, $C_1$-$C_6$-alkyl, $C_1$-$C_6$-alkylcarbonyl, $C_1$-$C_6$-alkylamino, formyl, hydroxycarbonyl, $C_1$-$C_6$-alkoxy, $C_1$-$C_6$-alkoxycarbonyl, $C_1$-$C_6$-alkylthio, $C_1$-$C_6$-alkylcarbonylamino, $C_1$-$C_4$-alkylsulphonylamino, $C_3$-$C_8$-cycloalkylcarbonylamino, pyrrolyl, $C_1$-$C_6$-alkylaminocarbonylamino, morpholinyl, oxypiperidinyl, oxopyrrolidinyl, oxomorpholinyl, pyrrolidinyl, morpholinylcarbonyl, piperidinyl, pyridinyl,

dihydropyrrolylcarbonyl, $C_1$-$C_4$-alkylpiperizinylcarbonyl, isoxazolecarbonylamino, tetrahydrofuranylcarbonylamino, furoylamino, piperidinylcarbonyl, or piperidinylcarbonyl ,

where $C_1$-$C_6$-alkyl may optionally be substituted by hydroxyl, amino, $C_1$-$C_6$-alkylaminocarbonylamino, $C_1$-$C_6$-alkylaminocarboxyl, morpholinyl or aryl,and

$C_1$-$C_6$-alkylcarbonylamino may optionally be substituted by $C_1$-$C_6$-alkoxy,

A is oxygen or sulphur,

the ring B is benzo or pyrido, each of which are optionally substituted by radicals from the series halogen, cyano, formyl, trifluoromethyl, trifluoromethoxy, nitro, amino, $C_1$-$C_6$-alkyl and $C_1$-$C_6$-alkoxy,

and

E is C≡C, phenylene, thienylene, oxadizolylene, pyrrolylene, furanylene, pyrimidinylene, or pyridinylene wherein each ring system respectively is optionally substituted by radicals from the series halogen, cyano, trifluoromethyl, trifluoromethoxy, nitro, amino, $C_1$-$C_6$-alkoxy and $C_1$-$C_6$-alkyl,

or a salt thereof.

5. (Previously Presented) The compound of formula (I) of Claim 1, in which

$R^1$ is 1-azabicyclo[2.2.2]oct-3-yl,

$R^2$ is hydrogen or $C_1$-$C_6$-alkyl,

$R^3$ is hydrogen, halogen or $C_1$-$C_6$-alkyl,

$R^4$ is hydrogen, halogen, cyano, trifluoromethyl, trifluoromethoxy, $C_1$-$C_6$-alkyl, $C_1$-$C_6$-alkoxy morpholinyl, piperidinyl or pyrrolidinyl, where alkyl is optionally substituted by a hydroxyl radical,

A is oxygen or sulphur,

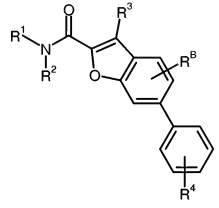
the ring B is benzo or pyrido, each of which are optionally substituted by radicals from the series halogen, cyano, trifluoromethyl, trifluoromethoxy, nitro, amino, $C_1$-$C_6$-alkyl and $C_1$-$C_6$-alkoxy,

and

E is C≡C, phenylene, thienylene, oxadizolylene, pyrrolylene, furanylene, pyrimidinylene, or pyridinylene wherein each ring system respectively is optionally substituted by radicals from the series halogen, cyano, trifluoromethyl, trifluoromethoxy, nitro, amino, $C_1$-$C_6$-alkyl and $C_1$-$C_6$-alkoxy,

or a salt thereof.

6. (Previously Presented) The compound of claim 1 having the formula (Ia)



(Ia),

in which

$R^1$ is (3*R*)-1-azabicyclo[2.2.2]oct-3-yl,

$R^2$ and $R^3$ are, independently of one another, hydrogen or methyl,

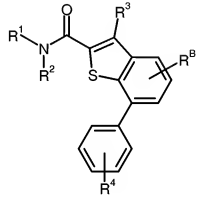
$R^4$ is hydrogen, halogen, cyano, trifluoromethyl, trifluoromethoxy, $C_1$-$C_6$-alkyl, $C_1$-$C_6$-alkoxy or morpholinyl, piperidinyl or pyrrolidinyl, where alkyl is optionally substituted by a hydroxyl radical,

and

$R^B$ is hydrogen, halogen, cyano, trifluoromethyl, trifluoromethoxy, nitro, amino, $C_1$-$C_6$-alkyl or $C_1$-$C_6$-alkoxy,

or a salt thereof.

7. (Previously Presented) The compound of claim 1 having the formula (Ib)



(Ib),

in which

$R^1$ is (3*R*)-1-azabicyclo[2.2.2]oct-3-yl,

$R^2$ and $R^3$ are, independently of one another, hydrogen or methyl,

$R^4$ is hydrogen, halogen, cyano, trifluoromethyl, trifluoromethoxy, $C_1$-$C_6$-alkyl, $C_1$-$C_6$-alkoxy ~~or heterocyclyl~~ morpholinyl, piperidinyl or pyrrolidinyl, where alkyl is optionally substituted by a hydroxyl radical, and

$R^B$ is hydrogen, halogen, cyano, trifluoromethyl, trifluoromethoxy, nitro, amino, $C_1$-$C_6$-alkyl and $C_1$-$C_6$-alkoxy,

or a salt thereof.

8. (Previously Presented) The compound of Claim 1, wherein

$R^1$ is (3*R*)-1-azabicyclo[2.2.2]oct-3-yl,

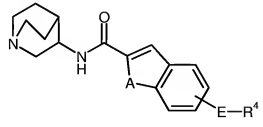
$R^2$ and $R^3$ are hydrogen,

$R^4$ is hydrogen, fluorine, chlorine, bromine, trifluoromethoxy, hydroxymethyl, methoxy or morpholinyl or piperidinyl, and

$R^B$ is hydrogen, halogen, cyano, trifluoromethyl, trifluoromethoxy or $C_1$-$C_4$-alkyl,

or a salt thereof.

9. (Previously Presented) The compound of claim 1 having the formula (Ic)

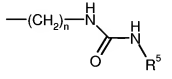



(Ic),

in which

E is phenylene,

$R^4$ is $C_1$-$C_6$-alkoxy, aminomethyl, hydroxycarbonyl, $C_3$-$C_8$-cycloalkylcarbonylamino, a group of the formula



where

$R^5$ is $C_1$-$C_6$-alkyl,

n is zero, 1, 2, 3 or 4,

or

morpholinyl, piperidinyl or pyrrolidinyl, which is optionally substituted by oxo,

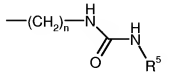
A is sulphur or oxygen,

or a salt thereof.

10. (Previously Presented) The compound of claim 9

E is phenylene,

$R^4$ is $C_1$-$C_4$-alkoxy, aminomethyl, hydroxycarbonyl, $C_3$-$C_6$-cycloalkylcarbonylamino, a group of the formula



,

where

$R^5$ is $C_1$-$C_4$-alkyl,

n is zero, 1 or 2,

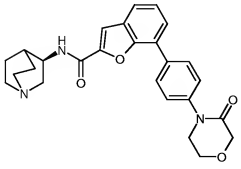
or

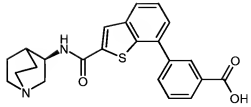
morpholinyl, piperidinyl or pyrrolidinyl, which is optionally substituted by oxo,

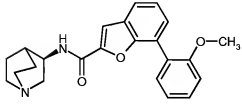
A is sulphur or oxygen,

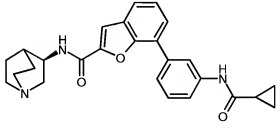
or a salt thereof.

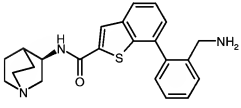
11. (Previously Presented) The compound of claim 1

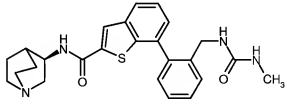




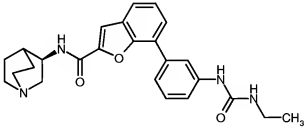








or



or a salt thereof.

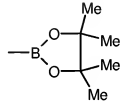
12. (Previously Presented) A process for the preparation of a compound of formula (I) of Claim 1, in which a compound of formula (II)

$$X^1\text{-}E\text{-}R^4 \quad \text{(II)},$$

in which

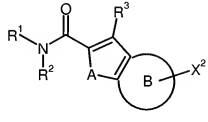
$R^4$ has the meanings indicated in Claim 1, and

$X^1$ is $-B(OH)_2$ or




in the case where E is arylene or heteroarylene, and is hydrogen in the case where E is -C≡C-,

is reacted with a compound of the formula (III)




(III),

in which

$R^1$, $R^2$, $R^3$, A and the ring B have the meanings indicated in Claim 1, and

$X^2$ is triflate or halogen, preferably chlorine, bromine or iodine,

and where appropriate

[A] the resulting compound of formula (I) is alkylated on the quinuclidine nitrogen atom with an appropriate alkylating reagent, or

[B] the resulting compound of formula (I) is oxidized on the quinuclidine nitrogen atom with a suitable oxidizing agent,

and the resulting compound of formula (I) is optionally converted to or a salt with an appropriate base or acid.

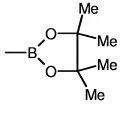
13. (Previously Presented) A process for the preparation of a compound of the formula (I) of Claim 1, in which a compound of formula (II)

$$X^1\text{-}E\text{-}R^4 \quad (II),$$

in which

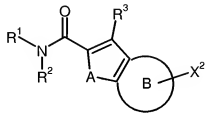
$R^4$ has the meanings indicated in Claim 1, and

$X^1$ is $-B(OH)_2$ or



in the case where E is arylene or heteroarylene, and is hydrogen in the case where E is -C≡C-,

is reacted with a compound of the formula (III)




(III),

in which

$R^1$, $R^2$, $R^3$, A and the ring B have the meanings indicated in Claim 1, and

$X^2$ is triflate or halogen, preferably chlorine, bromine or iodine,

and the resulting compound of formula (I) is optionally converted to a salt with an appropriate base or acid.

14. (Canceled)

15. (Previously Presented) A pharmaceutical composition comprising at least one compound according to any of Claims 1 to 11 and at least one pharmaceutically acceptable, essentially nontoxic carrier or excipient.

16. (Canceled)

17. (Canceled)

18. (Canceled)

19. (Previously Presented) A method for the treatment or prophylaxis of impairments of perception, concentration, learning and/or memory comprising administering to a human or animal at least one compound according to any of Claims 1 to 11.

## REMARKS

Claims 1-13, 15 and 19 are pending in this application. No amendments have been made to the claims.

Applicants respectfully reserve the right to pursue any non-elected, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

Reconsideration and withdrawal of the objections to and the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the application is in condition for allowance.

***Interview Summary***

Applicants respectfully thank the Examiner for participating with Attorney Nicholas J. DiCeglie, Jr. (Registration No. 51,615) in a telephonic interview on December 13, 2010. During the interview, the Examiner and Mr. DiCeglie discussed the possibility of overcoming the remaining Double Patenting rejection by deletion of the term "phenylene" from the definition of "E." The Examiner noted that the deletion of the term "phenylene" would cause some dependent claims to no longer have antecedent basis and, thus, those dependent may need to be canceled. The Examiner suggested the claims should be allowable without amendment upon filing of a terminal disclaimer. No final agreement was reached.

Applicants respectfully thank the Examiner for being amenable to such an addition to the restriction groups.

***Rejections for Non-Statutory Double Patenting***

Claims 1-9 and 15 stand rejected on the grounds of nonstatutory obviousness-type double patenting over Claims 1-5 of United States Patent No. 7,732,477. The Examiner has based this

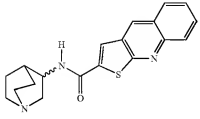
rejection on his conclusion that the term "benzo" as used in claim 1 of U.S. Patent No. 7,732,477 as a substituent for ring B of Formula I refers to a "phenyl" substituent. Applicants respectfully disagree.

The relevant portion of claim 1 reads as follows: "the ring B represents benzo, pyrimido, pyrimidazo or pyridazione which is substituted by a radical selected from the group consisting of halogen ... and benzo." It is the second occurrence of the term benzo in this passage which the Examiner concludes means "phenyl". The Examiner appears to have come to this conclusion regarding the second occurrence of the term benzo because, according to the Examiner, the "closest definition found in the specification of U.S. Patent No. 7,732,477 regarding the term benzo is found on page 6 ... where the term phenylcarbonyl radical corresponds to benzoyl radical;" and " [i]n the chemical community, the term "benzo" is commonly referred and related to the term "phenyl"." Again, Applicants respectfully disagree.

Applicants contend that the term "benzo" as used in of U.S. Patent No. 7,732,477 has a consistent definition within the specification. Specifically, claim 1 specifies that ring B can be "benzo". Thus, ring B together with the 5-membered ring to which it is fused can form, for example, a benzofuran or benzothiophene. Accordingly, "benzo" refers to a bivalent group that attaches to the 5-membered ring to form a 6-membered ring fused to the 5-membered ring in the fused ring system. Thus, Applicants contend that the term second occurrence of the term "benzo" must be read consistently to refer to a bivalent group that attaches to a ring system to form a 6-membered ring fused to the remainder of the ring system. Indeed, this definition is consistent with the Examples. Examples 12, 48 and 49, which are depicted below, are all examples in which ring B is benzo substituted with a benzo group.

EXAMPLE 12

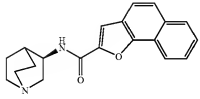
N-(1-Azabicyclo[2.2.2]oct-3-yl)thieno[2.3-b]quinoline-2-carboxamide hydrochloride



x HCl

EXAMPLE 48

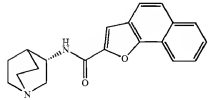
N-[(3R)-1-Azabicyclo[2.2.2]oct-3-yl]naphtho[1,2-b]furan-2-carboxamide hydrochloride



x HCl

EXAMPLE 49

N-[(3S)-1-Azabicyclo[2.2.2]oct-3-yl]naphtho[1,2-b]furan-2-carboxamide hydrochloride



x HCl

The passage on page 6 referred to by the Examiner, while providing an understanding of the term "benzoyl", does not refer to the term "benzo." While the term benzoyl is both commonly known and defined as phenylcarbonyl, the use of the term benzoyl does not equate the term "benzo" with the term "phenyl". Similarly, while the chemical community may readily recognize a "benzo" group and a "phenyl" group as having related ring structures, Applicants contend that the chemical community would not consider the term "benzo" and the term "phenyl" to be the same moiety under common naming conventions.

As such, Applicants contend that the Examiner has imported an inconsistent definition of the term "benzo" into the claims and that one of ordinary skill in the art, upon reading the specification as a whole would interpret the second occurrence of the term "benzo" consistently with the first occurrence. As such, Applicants contend that Claims 1-9 and 15 are not obvious over the Claims 1-5 of United States Patent No. 7,732,477 and that this rejection be reconsidered and withdrawn.

## CONCLUSION

In view of the foregoing remarks presented herein, reconsideration and withdrawal of all election requirements and allowance of the instant application with all pending claims are respectfully solicited. If a telephone conversation with Applicants' attorney(s) would help to expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned.

Applicants believe that no additional fees are required for consideration and entry of this paper. However, Applicants authorize the Director to charge any required fee or credit any overpayment to Deposit Account No. 04-1105, Reference No. 84804(303989).

Respectfully submitted,

Date: January 26, 2011

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